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SPECIFIC PROPHYLAXIS OF INFLUENZA IN THE USSR

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Influenza is one of the most widespread infectious diseases. It affects all age groups of the population. The fight against influenza is one of the most important practical tasks facing medical science and public health organs.

A successful solution of the task depends largely on timely application of all necessary prophylactic and antiepidemic measures.

Investigation of active immunization against influenza is being conducted along two basic lines, i.e., by working on the subcutaneous administration of killed vaccines, and by the creation of living vaccines for intranasal administration.

It has been established that subcutaneous inoculation with concentrated formol vaccine brings about a considerable increase in the titer of antibodies i . the blood of those inoculated. However, this method of immunization does not produce an equally pronounced increase in the titer of antibodies in the nasal secretion.

It has been found that intranasal immunization with concentrated formol vaccine is as effective as the method of subcutaneous administration. One must take into consideration that in intranasal immunization the sa coefficient of reduction of incidences of the disease is achieved by adminis ing only half as much vaccine as is necessary in subcutaneous immunization. The concentrated formol vaccine has substantial drawbacks, however. The principal drawbacks are the difficulty and high cost of producing the vaccine. The inconvenience of administering this vaccine subcutaneously must also be taken into consideration.

Under the circumstances, mass immunization with the use of this vaccine is not feasible. Soviet scientists have paid great attention to an investigation of the effectiveness of intranasal immunization with living influenza vaccines prepared from allantoic cultures of the viruses of types A, A1, and B. Experiments on animals demonstrated that this method of administering the vaccine is the most effective. Observations on the dynamics of the immunological shifts in human beings inoculated by this method have shown an increased accumulation of antibodies in the nasal secretion, which is the most reliable index of insusceptibility to influenza.

One must conclude on the basis of a number of observations that intranasal immunization with living vaccine produces a better effect than subcutaneous immunization with concentrated formol vaccine, although the latter contains eight to ten times more virus.

The effectiveness of inoculation prophylaxis depends not only on the quality of the vaccines applied, but also on the method by which they have been introduced into the organism. The last circumstance is of the greatest importance in infections affecting predominantly the respiratory tract, particularly in virus grippe infections.

At present, the method of active immunization with living influenza vaccine is being applied more and more extensively in practice. The complete safety of this preparation and the tolerance of patients to it have been established.

Intranasal immunization with living vaccine that has been prepared from attenuated strains of the influenza virus was found to bring about a number of insignificant changes of a functional character. A small number of those inoculated exhibit an insignificant rise in temperature. In more than half the patients thus affected, the temperature reaction is terminated toward the morning of the following day. In the remaining patients, the fever does not continue for longer than 24 hours. The same results were obtained by physicians who carried out the immunization with dry living vaccine. Tens of thousands of people have been observed after immunization with this type of vaccine.

Extensive application of living vaccine for purposes of immunization is possible if the influenza virus preserves for a long time the properties of infectiousness and immunogenicity. The liquid influenza vaccines used earlier have a short period of preservation, a circumstance which limited greatly the range of their practical application. It was necessary to find a method for the preparation of dry, stable vaccine.

Investigations carried out on the subject established that in the drying of the virus the medium in which the virus is dried is of decisive importance. It was established that a saccharose egg yolk medium is the best among those investigated. If this medium is used, the viability of the virus and its infectious, antigenic, and immunogenic properties are preserved during the drying process as well as during prolonged storage in a dry state.

Our investigations over many years have culminated in a new preparation -- a dry, living influenza vaccine consisting of the virus types known at present (A, A_1, and B). The viruses contained in the vaccine have a weakened virulence toward human beings. The technology of mass production of the vaccine has been developed. The methods that have been developed assure the production of a preparation which has uniform properties and preserves its infectious and immunogenic activity for 2 years. The period of usefulness of the vaccine presumably exceeds 2 years.

One of the advantages of dry vaccine is its stability during transportation over long distances under ordinary temperature conditions. The dry vaccine is dissolved in distilled or cold boiled water and is then introduced into the respiratory tract by means of an atomizer or into the nose by means of an eye dropper.

A. A. Smorodintsev proposed that the dry virus be mixed with starch, penicillin, and sulfa drugs and then introduced into the upper respiratory tract in the dry state by means of a powder blower.

The drying of vaccine strains under definite conditions permits their preservation in a state necessary for obtaining an immunogenic vaccine with the necessary degree of attenuated virulence toward human beings.

The principal criterion for the prophylactic value of living influenza vaccine is the epidemiological effectiveness of the immunization achieved with the vaccine. Epidemiological observations on a large number of people established the reduction of the incidence of influenza among those inoculated.

The date obtained at the end of 1953 by M. I. Sokolov, S. S. Unanov, V. A. Kudryavtsev, A. K. Alekseyeva, and K. S. Kulikova testified to the great effectiveness of the inoculations.

The inoculations were carried out with the dry, living polytype vaccine (types A, A_1, and B) which has been perfected recently and prepared at the Moscow Institute of Vaccines and Sera imeni Mechnikov. The vaccine was administered intranasally in a single application. The epidemiological conditions were characterized by a rapid and extensive spreading of the incidence of influenza.

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Statistics among those affected by influenza established that the incidence of influenza and acute catarrhs of the upper respiratory tract comprised 24.5% among those who had not been inoculated, while it was 4.3% among those inoculated.

On the basis of clinical diagnosis carried out separately in the two groups, the incidence of influenza among those inoculated was found to be five or more times lower than among those not inoculated. The analysis of the effectiveness of the inoculation at various targets has shown that lowering of the incidence of infection among those inoculated could be expressed by a factor of 4 to 10. Data on the dynamics of the morbidity show that, while the number of infections among those not inoculated continued to rise sharply, it did not rise among those inoculated, but on the contrary, was reduced soon after inoculation.

The data cited above, which show the advantages of the dry, living influenza vaccine and of the intranasal method of immunization, give reason to believe that the new method of prophylactic vaccination developed by Soviet scientists is an effective measure for combating influenza. Even a reduction of the morbidity by a factor of 2 expresses much larger prophylactic effectiveness as far as the number of people actually protected against the infection is concerned.

In investigating the effectiveness of the inoculation, usually only one half or a smaller fraction of all persons observed at any one target was immunized. The presence of a large number of nonimmunized people in the group increases the frequency of contacts between healthy and sick people and increases the concentration of the virus in the group, thus contributing to the possibility that the immunity of those inoculated may be overcome. The data obtained in the investigations show distinctly that timely mass immunization of a group followed by an annual reinoculation results in a much more effective prevention of the disease than that obtained by an experimental partial inoculation of members of the group. These data permit the conclusion that the degree of reduction of the incidence of influenza depends directly on the degree of completeness of the inoculation carried out among members of the group.

Further progress in the field of intranasal immunization with dry, living vaccine may be secured if, on the one hand, the immunization characteristics are improved by selecting more highly immunogenic strains and if, on the other hand, the method of application is perfected. Of decisive importance will be the systematic application of inoculations on a mass scale.

Application of the anti-influenza serum proposed by A. A. Smorodintsev furnishes an effective method for the prophylaxis of influenza and supplements active immunization. Administration of this serum is indicated when an influenza outbreak has already begun. The serum is introduced into the respiratory tract in a dry or liquid state, either by inhalation or by means of an atomizer. It is administered every 5-7 days. According to Smorodintsev's observations, serum prophylaxis lowers the incidence of influenza by a factor of 3 or more.

One may state that, after a period of temporary failures, investigation of the problem of specific prophylaxis of influenza has begun to yield good results. The experience in the production of dry, living influenza vaccine and of the anti-influenza serum has shown that all necessary prerequisites for their production exist. In the USSR, where there is an extensive network of institutes of vaccines and sera, the organization of the mass production of these preparations is entirely feasible. Consequently, the fight against influenza by active immunization and serum prophylaxis must be regarded as a current task of the public health organs.

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